C3 cancelled

73. (New) The composition according to claim 37, wherein the concentration of second or third generation antidepressant in said composition falls in the range of about 0.5 up to 10 wt %.

Remarks

Courtesies extended to Applicant Sawynok, Applicants' representative and a representative of the licensee, Epicept, at the personal interview held August 7, 2002, are acknowledged with appreciation.

As discussed at the personal interview, the present invention provides compositions containing second or third generation antidepressants, formulated for topical application, or for local injection. Invention compositions have been shown to produce local analgesia in subjects having a site of local discomfort. Invention formulations possess the advantage of providing a higher and more efficacious concentration of antidepressant to the region of the sensory nerve terminal than is achievable with systemic administration of the same antidepressant. In addition, invention compositions for local administration greatly reduce the side effects that may result from systemic administration of antidepressants.

By the present communication, claims 26, 37 and 49 have been amended, and new claims 72 and 73 have been added to define Applicants' invention with greater particularity. These amendments and new claims add no new matter as they are fully supported by the specification and original claims. The amendments and new claims submitted herewith are respectfully submitted to place the application in condition for allowance, or as a minimum, in better condition for appeal. Accordingly, entry of the amendments submitted herewith is respectfully requested. For the Examiner's convenience, a marked up version of the changes made to the claims is provided herewith, labeled as APPENDIX A. Upon entry of the amendments submitted herewith, claims 26, 37-44, 49-53 and 72-73 will be pending. For the Examiner's convenience a clean copy of all pending claims is provided herewith as APPENDIX B.

The rejection of claim 26 under 35 U.S.C. § 112, first paragraph, is respectfully traversed. As discussed at the personal interview, Applicants have obviated this rejection by re-writing claim 37 as an independent claim, including all the requirements of claim 26. In view of the Examiner's acknowledgment that the specification is enabling for second or third generation antidepressants as set forth in claim 37 (see page 2, lines 13-15 of the Office Action, Paper No. 15), it is respectfully submitted that this rejection is not applicable to claim 37, as amended.

It is respectfully submitted that this rejection is also inapplicable to amended claim 26, which now recites specific compounds which fit within the definition of second or third generation antidepressants. See, for example, page 19, lines 12-14 of Applicants' specification, as well as Goodman and Gilman at page 464 (incorporated by reference by the present specification, see page 22, lines 8-13) for support for these amendments to claim 26.

The rejection of claims 26, 37-44 and 49-51 under 35 U.S.C. § 102(e) as allegedly being anticipated by Smith et al., U.S. Patent No. 5,922,341, (hereinafter referred to as "Smith") is respectfully traversed. As discussed at the personal interview, Smith is respectfully submitted to be unavailable as prior art. It is respectfully submitted that the original declaration submitted on February 22, 2002, is more than adequate to overcome Smith.

As discussed at the personal interview, the original declaration made reference in paragraph 5 to the broad concept of using an antidepressant for local administration. There was no limitation contemplated as to the class of antidepressant for such use. Further discussion in the declaration, especially at paragraphs 6 and 7, make explicit reference to the use of a prototype antidepressant (i.e., amitriptyline) for the initial studies. The fact that a member of a specific class of antidepressants was used as the first example tested in no way limits the scope of compounds contemplated by the inventors.

In order to further amplify the point addressed above, Applicants provide herewith a supplemental declaration which provides additional detail relating to the conception of the invention. As discussed at the personal interview, it is respectfully submitted that the

supplemental declaration removes all doubt as to Applicants' ability to remove Smith as a reference.

Since Smith is not properly applied against the present claims, reconsideration and withdrawal of the rejection are respectfully requested.

The rejection of claims 26, 37-44 and 49-51 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Smith et al., is respectfully traversed. In view of the inapplicability of the Smith reference, as discussed above, this rejection is respectfully submitted to be without merit. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

The rejection of claims 52-53 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Smith et al., in view of Kitchell et al., U.S. Patent No. 5,486,362, is respectfully traversed. As above, in view of the inapplicability of the Smith reference, this rejection is respectfully submitted to be without merit. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

To address an additional issue raised by the Office for the first time at the personal interview, claims 72 and 73 have been introduced herewith, providing concentration ranges applicable to invention compositions. Support for these values is provided, for example, in texts known to those of skill in the art, for example Goodman and Gilman's The Pharmacological Basis of Therapeutics, and Remington's Pharmaceutical Sciences, incorporated by reference in the specification (see specification at page 22). As readily recognized by those of skill in the art, these are concentration ranges which are consistent only with formulations prepared specifically for topical and/or local administration.

In view of the above amendment and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date: August 20, 2002

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Enclosures: Appendices A and B

APPENDIX A – AMENDED CLAIMS

VERSION WITH MARKINGS TO SHOW CHANGES MADE

26. (Amended) A composition for local administration comprising a second or third generation antidepressant, and a vehicle suitable for **[~~topical~~]** **local** administration**, wherein the second or third generation antidepressant is selected from the group consisting of amoxapine, desipramine, maprotiline, nortriptyline, protriptyline, trazodone, bupropion, mirtazapine, venlafaxine, nefazodone, reboxetine, and fluoxetine.**

37. (Amended) **[~~The~~]** **A** composition **[~~according to claim 26~~]** **for local administration comprising a second or third generation antidepressant, and a vehicle suitable for local administration,** wherein the second or third generation antidepressant has a structure:

$$Ar_3(Y)\text{-}X\text{-}Ar_4(Q)$$

wherein Ar_3 is a substituted N-containing heterocyclic ring,

Y is either an aryl group fused to the heterocyclic ring, or one or two substituents selected from the group consisting of alkyl, alkyloxy, arylalkyl, arylalkyloxy, aryl, heteroaryl substituents, and combinations thereof comprising a total of about 4 to 8 carbons attached to Ar_3,

X is an alkyl group comprising 2 to 5 carbon atoms linking Ar_3 and Ar_4,

Ar_4 is a piperazine attached to X by a first nitrogen atom of Ar_4, and

Q is a benzene ring optionally substituted with a biocompatible halogen and attached to Ar_4 at a second nitrogen atom of Ar_4.

49. (Amended) The composition according to claim 26 in a formulation selected from the group consisting of a cream, a lotion, a gel, an ointment, a spray, a **[~~powder~~]** **patch**, a polymer stabilized crystal, and an aerosol.

APPENDIX B – COMPLETE SET OF PENDING CLAIMS

26. (Amended) A composition for local administration comprising a second or third generation antidepressant, and a vehicle suitable for local administration, wherein the second or third generation antidepressant is selected from the group consisting of amoxapine, desipramine, maprotiline, nortriptyline, protriptyline, trazodone, bupropion, mirtazapine, venlafaxine, nefazodone, reboxetine, and fluoxetine.

37. (Amended) A composition for local administration comprising a second or third generation antidepressant, and a vehicle suitable for local administration, wherein the second or third generation antidepressant has a structure:

$$Ar_3(Y)\text{-}X\text{-}Ar_4(Q)$$

wherein Ar_3 is a substituted N-containing heterocyclic ring,

Y is either an aryl group fused to the heterocyclic ring, or one or two substituents selected from the group consisting of alkyl, alkyloxy, arylalkyl, arylalkyloxy, aryl, heteroaryl substituents, and combinations thereof comprising a total of about 4 to 8 carbons attached to Ar_3,

X is an alkyl group comprising 2 to 5 carbon atoms linking Ar_3 and Ar_4,

Ar_4 is a piperazine attached to X by a first nitrogen atom of Ar_4, and

Q is a benzene ring optionally substituted with a biocompatible halogen and attached to Ar_4 at a second nitrogen atom of Ar_4.

38. (Reiterated) The composition according to claim 37 wherein the X is an alkyl group containing 3 carbons.

39. (Reiterated) The composition according to claim 37 wherein Ar_3 is a 1,2,4-triazone substituted at the 4 position with the arylalkyoxy substituent containing 6 to 8 carbon atoms.

40. (Reiterated) The composition according to claim 39 wherein the heteroarylalkyl substituent contains an oxygen atom.

41. (Reiterated) The composition according to claim 37 wherein the benzene ring is substituted with a halogen selected from the group consisting of chlorine, bromine, and fluorine.

42. (Reiterated) The composition of claim 26 further comprising an inert carrier.

43. (Reiterated) The composition of claim 42 wherein the inert carrier is selected from the group consisting of water, isopropyl alcohol, gaseous fluorocarbons, ethyl alcohol, polyvinyl pyrrolidone, propylene glycol, a fragrance, a gel-producing material, stearyl alcohol, stearic acid, spermaceti, sorbitan monooleate, methylcellulose, and suitable combinations of any two or more thereof.

44. (Reiterated) The composition according to claim 26 wherein the composition further comprises a penetration enhancing agent.

49. (Amended) The composition according to claim 26 in a formulation selected from the group consisting of a cream, a lotion, a gel, an ointment, a spray, a patch, a polymer stabilized crystal, and an aerosol.

50. (Reiterated) The composition of claim 26 further comprising a neutralizing agent.

51. (Reiterated) The composition of claim 26 wherein the composition is formulated for local injection.

52. (Reiterated) The composition according to claim 26 wherein the antidepressant is encapsulated in a slow release delivery vehicle.

53. (Reiterated) The composition according to claim 52 wherein the delivery vehicle is selected from the group consisting of a liposome, a microcapsule, and a polymer stabilized crystal.

72. (New) The composition according to claim 26, wherein the concentration of second or third generation antidepressant in said composition falls in the range of about 0.5 up to 10 wt %.

73. (New) The composition according to claim 37, wherein the concentration of second or third generation antidepressant in said composition falls in the range of about 0.5 up to 10 wt %.